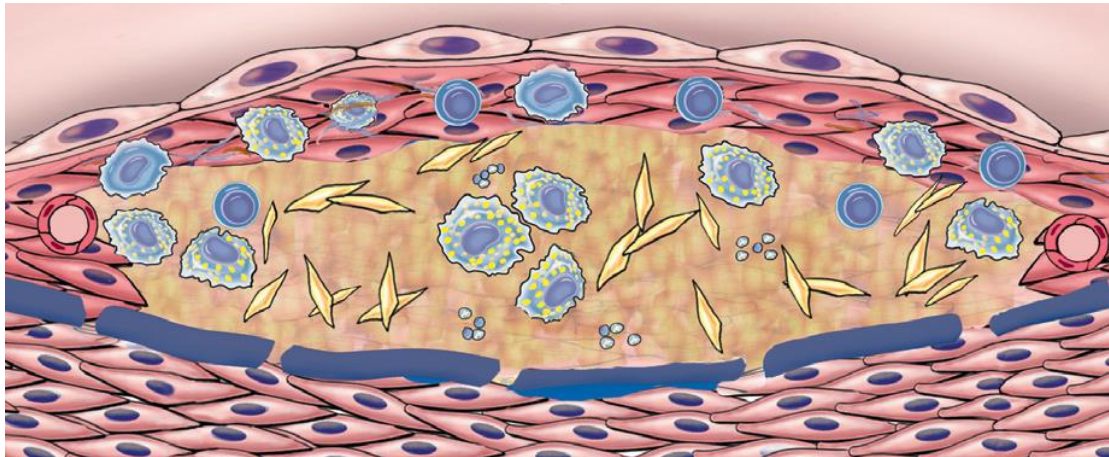


ATHEROSCLEROSIS

Atherosclerosis is characterized by the presence of intimal lesions called *atheromas* (or *atheromatous* or *atherosclerotic plaques*).

Atheromatous plaques are raised lesions composed of soft grumous lipid cores (mainly cholesterol and cholesterol esters, with necrotic debris) covered by fibrous caps.



Atherosclerotic plaques can mechanically obstruct vascular lumina and are prone to rupture, resulting in catastrophic vessel thrombosis.

Epidemiology of Atherosclerosis

Atherosclerosis is virtually ubiquitous among most developed nations

The mortality rate for IHD in the United States is among the highest in the world,

The prevalence and severity of atherosclerosis and IHD have been correlated with a number of risk factors;

(i.e., hyperlipidemia, hypertension, and smoking),

Constitutional Risk Factors

- *Genetics*. Family history is the most important independent risk factor for atherosclerosis.

- *Age*

- *Gender.*
- *Hyperlipidemia*—and, more specifically, *hypercholesterolemia*—

is a major risk factor for development of atherosclerosis and is sufficient to induce lesions in the absence of other risk factors.

The main cholesterol component associated with increased risk is low-density lipoprotein (LDL) cholesterol (“bad cholesterol”); LDL distributes cholesterol to peripheral tissues.

By contrast, high-density lipoprotein (HDL) (“good cholesterol”) mobilizes cholesterol from developing and existing vascular plaques and transports it to the liver for biliary excretion.

Consequently, higher levels of HDL correlate with reduced risk.

- *Hypertension*
- *Cigarette smoking*
- *Diabetes mellitus*

PATHOGENESIS

Historically, there have been two dominant theories regarding atherogenesis; one emphasizing intimal cellular proliferation in response to endothelial injury, and the other focusing on repeated formation and organization of thrombi.

According to this , atherosclerosis results from the following pathogenic events:

- **Endothelial injury**—and resultant endothelial dysfunction—leading to increased permeability, leukocyte adhesion, and thrombosis
- **Accumulation of lipoproteins** (mainly oxidized LDL and cholesterol crystals) in the vessel wall
- **Platelet adhesion**

- **Monocyte adhesion to the endothelium**, migration into the intima, and differentiation into **macrophages** and **foam cells**
- **Lipid accumulation** within macrophages, which release inflammatory cytokines
- **Smooth muscle cell recruitment due to factors released** from activated platelets, macrophages, and vascular wall cells
- **Smooth muscle cell proliferation and ECM production.**

Hypertension

Definition

Hypertension (HTN or HT), also known as *high blood pressure (HBP)*, is a long-term medical condition in which the blood pressure in the arteries is persistently elevated.

High blood pressure typically does not cause symptoms. Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia.

High blood pressure is classified as *primary (essential)* hypertension or *secondary* hypertension.

About 90–95% of cases are *primary*, defined as high blood pressure due to nonspecific lifestyle and genetic factors. Lifestyle factors that increase the risk include excess salt in the diet, excess body weight, smoking, and alcohol use.

The remaining 5–10% of cases are categorized as *secondary* high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.

Blood pressure is classified by *two measurements*, the *systolic* and *diastolic* pressures, which are the maximum and minimum pressures, respectively.

For most adults, normal blood pressure at rest is within the range of 100–130 millimeters mercury (mmHg) systolic and 60–80 mmHg diastolic.

For most adults, high blood pressure is present if the resting blood pressure is persistently at or above 130/80 or 140/90 mmHg.

Signs and symptoms

Some people with high blood pressure report headaches (particularly at the back of the head and in the morning), as well as lightheadedness, vertigo, tinnitus (buzzing or hissing in the ears), altered vision or fainting episodes. These symptoms, however, might be related to associated anxiety rather than the high blood pressure itself.

Secondary hypertension

Hypertension due to an identifiable cause. For example,

Cushing's syndrome.

Hyperthyroidism

Renal artery stenosis

Hypertensive crisis

Severely elevated blood pressure (equal to or greater than a systolic 180 or diastolic of 110) is referred to as a hypertensive crisis.

Causes

Primary hypertension

➤ genome-wide association studies (GWAS) have identified 35 genetic loci related to blood pressure; 12 of these genetic loci influencing blood pressure were newly found.

➤ Blood pressure rises with aging when associated with a western diet and lifestyle and the risk of becoming hypertensive in later life is significant.

- vitamin D deficiency are less clear.
- Insulin resistance, which is common in obesity and is a component of syndrome X (or the metabolic syndrome), also contributes to hypertension.
- low birth weight, maternal smoking, and lack of breastfeeding may be risk factors for adult essential hypertension.
- An increased rate of high blood uric acid has been found in untreated people with hypertension in comparison with people with normal blood pressure.
- Periodontal disease is also associated with high blood pressure.

Management

Lifestyle modifications

The first line of treatment for hypertension is lifestyle changes, including dietary changes, physical exercise, and weight loss.

Medications

Several classes of medications, collectively referred to as antihypertensive medications, are available for treating hypertension.

First-line medications for hypertension include thiazide-diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors (ACE inhibitors), and angiotensin receptor blockers (ARBs).

Resistant hypertension

Resistant hypertension is defined as high blood pressure that remains above a target level, in spite of being prescribed three or more antihypertensive drugs simultaneously with different mechanisms of action. Failing to take prescribed medications as directed is an important

cause of resistant hypertension. Resistant hypertension may also result from chronically high activity of the autonomic nervous system, an effect known as "**neurogenic hypertension**".

Refractory hypertension

Refractory hypertension is characterized by uncontrolled elevated blood pressure unmitigated by five or more antihypertensive agents of different classes, including a long-acting thiazide-like diuretic, a calcium channel blocker, and a blocker of the renin-angiotensin system. People with refractory hypertension typically have increased sympathetic nervous system activity, and are at high risk for more severe cardiovascular diseases and all-cause mortality.